PATENT COOPERATION TREATY

| From the I | NTERNATIONAL | BUREAU |
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NOTIFICATION OF ELECTION

(PCT Rule 61.2)

То

Assistant Commissioner for Patents United States Patent and Trademark Office Box PCT Washington, D.C.20231 ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year) 02 May 2000 (02.05.00)

BANDMAN, Olga et al

in its capacity as elected Office

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|--|--|--|--|
| International application No. PCT/US99/16164 | Applicant's or agent's file reference PF-0559 PCT | | |
| International filing date (day/month/year) 16 July 1999 (16.07.99) | Priority date (day/month/year) 16 July 1998 (16.07.98) | | |
| Applicant | | | |

| 1. | The designated Office is hereby notified of its election made: |
|----|---|
| | X in the demand filed with the International Preliminary Examining Authority on: |
| | 08 February 2000 (08.02.00) |
| | in a notice effecting later election filed with the International Bureau on: |
| | |
| 2. | The election X was |
| | was not |
| | made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b). |
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The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland

Authorized officer

Olivia RANAIVOJAONA

Telephone No.: (41-22) 338.83.38

Facsimile No.: (41-22) 740.14.35

PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

| Applicant's or agent's file reference PF-0559 PCT | FOR FURTHER ACTIO | See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416) | |
|--|---|---|--|
| International application No. | International filing date (day/ | month/year) | Priority date (day/month/year) |
| PCT/US99/16164 | 16 JULY 1999 (16.07.1999) | | 16 JULY 1998 (16.07.1998) |
| International Patent Classification (IPC) | | C | |
| IPC(7): C07K 1/00 and US Cl.: 530/350 | | | |
| Applicant | | | |
| INCYTE PHARMACEUTICALS INC. | | | |
| | ary examination report has lis transmitted to the applican | | this International Preliminary |
| 2. This REPORT consists of | a total of 3 sheets, including | this cover sheet | |
| which have been ame | nded and are the basis for th | is report and/or | description, claims and/or drawings sheets containing rectifications made inistrative Instructions under the PCT). |
| These annexes consist of a | total of sheets. | | |
| 3. This report contains indica | tions relating to the following | ng items: | |
| l Basis of the repo | ort | | |
| II Priority | | | |
| III Non-establishme | ent of report with regard to i | novelty, inventiv | e step and industrial applicability |
| IV Lack of unity of | finvention | | |
| · — | V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement | | |
| VI Certain docume | VI Certain documents cited | | |
| VII Certain defects | VII Certain defects in the international application | | |
| VIII Certain observations on the international application | | | |
| | | | |
| Date of submission of the demand | Da | ate of completion | of this report |
| 08 February 2000 (08.02.2000) | | A | |
| Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703)305-3230 Authorized officer Ulrike Winkler, Ph.D. Pelephone No. 703-308-0196 | | <i>[</i>] | |

Form PCT/IPEA/409 (cover sheet)(July 1998)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

| International application No. | |
|-------------------------------|--|
| PCT/US99/16164 | |

| I. | Basis of the report |
|-----|--|
| 1. | With regard to the elements of the international application:* |
| | the international application as originally filed. |
| | the description: |
| | pages 1-50 as originally filed |
| | pages NONE, filed with the demand |
| | pages NONE , filed with the letter of |
| | the claims: |
| | pages 51 and 52 , as originally filed |
| | pages NONE , as amended (together with any statement) under Article 19 pages NONE , filed with the demand |
| | pages NONE , filed with the definance . pages NONE , filed with the letter of |
| | the drawings: |
| | pages 1-17 , as originally filed |
| | pages NONE, filed with the demand |
| | pages NONE, filed with the letter of |
| | the sequence listing part of the description: |
| | pages 1-7, as originally filed |
| | pages NONE , filed with the demand |
| | pages NONE , filed with the letter of |
| 2. | With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item. These elements were available or furnished to this Authority in the following language which is: |
| | the language of a translation furnished for the purposes of international search (under Rule23.1(b)). |
| | the language of publication of the international application (under Rule 48.3(b)). |
| | the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3). |
| 3. | With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing: |
| | contained in the international application in printed form. |
| | filed together with the international application in computer readable form. |
| | furnished subsequently to this Authority in written form. |
| | furnished subsequently to this Authority in computer readable form. |
| | The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished. |
| | The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished. |
| 4. | The amendments have resulted in the cancellation of: |
| | the description, pages NONE |
| | the claims, Nos. NONE |
| | the drawings, sheets/fig NONE |
| 5. | |
| | beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).** Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in |
| thu | is report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17). * Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report. |
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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/16164

| III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability | | |
|---|---|--|
| 1. The | e question whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or see industrially applicable have not been and will not be examined in respect of: | |
| | the entire international application, | |
| \boxtimes | claims Nos. 15-18 | |
| | Ciamis 103. <u>15-16</u> | |
| becar | use: | |
| | the said international application, or the said claim Nos relate to the following subject matter which does not require international preliminary examination (specify): | |
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| | the description, claims or drawings (indicate particular elements below) or said claims Nos are so unclear that no meaningful opinion could be formed (specify): | |
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| | the claims, or said claims Nos are so inadequately supported by the description that no meaningful opinion could be formed. | |
| \boxtimes | no international search report has been established for said claims Nos. 15-18 | |
| 2. A me seque | aningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid nee listing to comply with the standard provided for in Annex C of the Administrative Instructions: | |
| | the written form has not been furnished or does not comply with the standard. | |
| | the computer readable form has not been furnished or does not comply with the standard. | |

Form PCT/IPEA/409 (Box III) (July 1998)

Inter anal Application No
PCT/US 99/16164

| A. CLASSIF IPC 7 | C12N15/53 C12N9/02 C12N5/16 C07K16/28 | A61K48/00 | C12Q1/68 |
|-----------------------------------|--|---|---|
| According to | International Patent Classification (IPC) or to both national classifica | tion and IPC | |
| B. FIELDS S | | | |
| Minimum doc IPC 7 | cumentation searched (classification system followed by classification C12N A61K C07K C12Q | in symbols) | |
| Documentati | on searched other than minimum documentation to the extent that s | uch documents are included in the | fields searched |
| Electronic da | ata base consulted during the international search (name of data bas | e and, where practical, search ter | ms used) |
| C. DOCUME | ENTS CONSIDERED TO BE RELEVANT | | |
| Category ° | Citation of document, with indication, where appropriate, of the rel | evant passages | Relevant to claim No. |
| A | GABRIELLI, F. ET AL.: " A nucle protein, synthesized in growth-a human hepatoblastoma cells, is member of the short-chain alcoho dehydrogenase family." EUR. J. BIOCHEM., vol. 232, no. 2, 1 September 1995 (1995-09-01), p 473-477, XP000862845 cited in the application the whole document | rrested a novel l | 1 |
| X Furt | ther documents are listed in the continuation of box C. | Patent family members | are listed in annex. |
| "A" docume consider filing (| ent which may throw doubts on priority claim(s) or | cited to understand the print invention "X" document of particular releva cannot be considered novel involve an inventive step wh | inflict with the application out ciple or theory underlying the lince; the claimed invention or cannot be considered to the document is taken alone |
| citatio "O" docum other "P" docum | is cited to establish the publication date of another on or other special reason (as specified) went referring to an oral disclosure, use, exhibition or means ent published prior to the international filing date but than the priority date claimed | document is combined with | oive an inventive step when the one or more other such docu- eing obvious to a person skilled |
| | actual completion of the international search | Date of mailing of the interna | |
| - | 5 January 2000 | 3 1. 03. 00 | |
| Name and | mailing address of the ISA European Patent Office, P.B. 5818 Patentiaan 2 NL - 2280 HV Rijswijk | Authorized officer | _ |
| | Tel. (+31-70) 340-2040, Tx. 31 651 epo ni, Fax:*(+31-70) 340-3016 | CHAMBONNET, | F |

INTERNATIONAL SEARCH REPORT



Inte tional Application No PUI/US 99/16164

| C.(Continu | ation) DOCUMENTS CONSIDERED TO BE RELEVANT | |
|-----------------------|---|-----------------------|
| Category ³ | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
| A | DONADEL, G. ET AL.: "Identification of a novel nuclear protein synthesized in growth-arrested human hepatoblastoma HepG2 cells." EUR. J. BIOCHEM. 195, 723-729, 1991, XP000863211 the whole document | 1 |
| P,X | FRANSEN M, VAN VELDHOVEN PP, SUBRAMANI S: "Identification of peroxisomal proteins by using M13 phage protein VI phage display: molecular evidence that mammalian peroxisomes contain a 2,4-dienoyl-CoA reductase." BIOCHEM JOURNAL, vol. 340, no. PT 2, 1 June 1999 (1999-06-01), pages 561-568, XP000862955 the whole document | 1,2 |

INTERNATIONAL SEARCH REPORT

Int _tional application No.

PCT/US 99/16164

| Box I | Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet) |
|-----------|---|
| This Inte | emational Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons: |
| 1. X | Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely: Remark: Although claims 17 and 18 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition. |
| 2. X | Claims Nos.: 15-16 because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically: see FURTHER INFORMATION sheet PCT/ISA/210 |
| 3. | Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a). |
| Box II | Observations where unity of invention is lacking (Continuation of item 2 of first sheet) |
| | mational Searching Authority found multiple inventions in this international application, as follows: |
| 1. | As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims. |
| 2. | As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee. |
| 3. | As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.: |
| · | No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: |
| Remark o | The additional search fees were accompanied by the applicant's protest. No protest accompanied the payment of additional search fees. |

INTERNATIONAL SEARCH REPORT

International Application No. PCT/US 99/16164

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 15 16

Present claims 15 and 16 relate to respectively an agonist and an antagonist of the polypeptide of claim 1 without giving true technical characterization. In consequence, the scope of said claims is ambiguous and vague, and their subject matter is not sufficiently disclosed and supported (Articles 5 and 6 PCT). No search can be carried out for such purely speculative claims whose wording is, in fact a mere recitation of the results to be achieved.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

1. Claim: partially 1 to 20

A substantially purified polypeptide comprising an amino-acid sequence consisting of SEQ ID NO:1, a variant having at least 90% amino acid identity or fragment thereof; an isolated and purified polynucleotide encoding said polypeptide, or comprising a sequence selected from the group consisting of SEQ ID NO:3, a fragment, a variant or a complementary polynucleotide thereof; an expression vector comprising said polynucleotide, a host cell comprising said vector and method of production using it; a pharmaceutical composition comprising said polypeptide and uses thereof, a purified antibody which specifically binds to said polypeptide, a purified agonist or antagonist of said polypeptide; methods for detecting such a polynucleotide.

2. Claim: partially 1 to 20

A substantially purified polypeptide comprising an amino-acid sequence consisting of SEQ ID NO:2, a variant having at least 90% amino acid identity or fragment thereof; an isolated and purified polynucleotide encoding said polypeptide, or comprising a sequence selected from the group consisting of SEQ ID NO:4, a fragment, a variant or a complementary polynucleotide thereof; an expression vector comprising said polynucleotide, a host cell comprising said vector and method of production using it; a pharmaceutical composition comprising said polypeptide and uses thereof, a purified antibody which specifically binds to said polypeptide, a purified agonist or antagonist of said polypeptide; methods for detecting such a polynucleotide.